

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding an isoform of a human calcium sensing receptor, wherein the nucleic acid comprises about 2922 to about 3003 nucleotides and has a deletion of about 231 nucleotides when compared to the wild-type form of the receptor as depicted in SEQ ID NO:11.
- 5 2. The nucleic acid according to claim 1, wherein said deletion is from the region encoding the extracellular domain of the receptor.
3. The nucleic acid according to claim 2, wherein the deletion is from about nucleotides 1075-1386 of SEQ ID NO:11.
4. The nucleic acid according to claim 2, wherein the deletion is from about nucleotides 1378-1608 of SEQ ID NO:11.
- 10 5. The nucleic acid according to claim 2, wherein the deletion is from about nucleotides 1075-1608 of SEQ ID NO:11.
6. The nucleic acid according to claim 1, having at least one property selected from
  - 15 a) it can be amplified by polymerase chain reaction (PCR) using an oligonucleotide primer derived from SEQ ID NO:7, SEQ ID NO:9 or SEQ ID NO:11;
  - b) it hybridizes under stringent conditions with a nucleic acid having a nucleotide sequence as depicted in SEQ ID NO:7 or SEQ ID NO:9; and
  - c) it encodes a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:8, SEQ ID NO:10, and allelic variants thereof.
- 20 7. The isolated nucleic acid of claim 2, wherein the isoform comprises an amino acid sequence as depicted in SEQ ID NO:8 or SEQ ID NO:10, or allelic variants thereof.
8. The isolated nucleic acid of claim 2 comprising a nucleotide sequence as depicted in SEQ ID NO:7 or SEQ ID NO:9, or allelic variants thereof.
9. The isolated nucleic acid of claim 1 wherein the nucleic acid can be amplified by polymerase chain reaction (PCR) using an oligonucleotide primer selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:6.
- 25 10. A vector comprising the nucleic acid of claim 1.
11. The vector according to claim 10 wherein the nucleic acid is operatively associated with an expression control sequence permitting expression of the receptor in an expression competent host cell.
- 30 12. The vector according to claim 11 selected from the group consisting of an RNA molecule, a plasmid DNA molecule, and a viral vector.
13. The vector according to claim 12 which is a plasmid DNA molecule.
14. The vector according to claim 12 which is a viral vector selected from the group consisting of

retrovirus, adenovirus, adeno-associated virus, herpes virus, and vaccinia virus.

15. A host cell transfected with the vector of claim 10.

16. A host cell transfected with the vector of claim 13.

5 17. The host cell of claim 15 selected from the group consisting of a bacterial cell, a yeast cell, and a mammalian cell.

18. A method for expressing an isoform of human calcium sensing receptor comprising:

a) culturing the host cell of claim 17 in culture medium under conditions permitting expression of the receptor; and

b) identifying cells expressing the receptor on their surface.

10 19. An isolated isoform of a human calcium sensing receptor, wherein the isoform comprises about 974 to about 1001 amino acids and has a deletion of about 77 amino acids when compared to the wild-type form of the receptor as depicted in SEQ ID NO:12.

20. The isoform according to claim 19, wherein said deletion is from the extracellular domain of the receptor.

15 21. The isoform according to claim 20, wherein the deletion is from about amino acids 358-462 of SEQ ID NO:12.

22. The isoform according to claim 20, wherein the deletion is from about amino acids 460-536 of SEQ ID NO:12.

20 23. The isoform according to claim 20, wherein the deletion is from about amino acids 358-536 of SEQ ID NO:12.

24. The isoform of claim 19, wherein the isoform comprises an amino acid sequence as depicted in SEQ ID NO:8 or SEQ ID NO:10, or allelic variants thereof.

25 25. A method of screening for agonists or antagonists of a CaSR isoform activity, the method comprising recombinantly producing a CaSR isoform, incubating a test sample with the CaSR isoform, measuring CaSR isoform activity and comparing the activity to that in the absence of the test sample.

26. The method according to claim 25, wherein the CaSR activity is its ability to influence intracellular calcium concentration.

30 27. The method according to claim 25, wherein the test sample is tested alone, in conjunction with an elevation in extracellular calcium concentration, or in the presence of other agonists or antagonists of CaSR isoform activity.

28. The method according to claim 26, wherein the intracellular calcium concentration is measured with a fluorescent indicator.

29. The method according to claim 28, wherein the indicator is fura-2.

35 30. A method of treating a patient suffering from a disease or disorder associated with abnormal

calcium levels, the method comprising the administration of a therapeutically effective amount of a compound capable of modulating the activity of a CaSR isoform.

31. The method according to claim 30, wherein the disease is hyperparathyroidism or osteoporosis.

5 32. The method according to claim 30, wherein the disease is Paget's disease, hypercalcemia malignancy, or hypertension.

33. The method according to claim 30, wherein the compound is an agonist or an antagonist of a CaSR isoform.

10 34. A method of increasing or decreasing the level of CaSR activity in a cell, the method comprising administering to the cell a nucleic acid capable of increasing or decreasing CaSR activity.

35. The method according to claim 34, wherein the cells are in a patient suffering from a disease or disorder associated with abnormal calcium levels.

36. The method according to claim 35, wherein the disease is hyperparathyroidism or osteoporosis.

15 37. The method according to claim 35, wherein the disease is Paget's disease, hypercalcemia malignancy, or hypertension.

38. The method according to claim 35, wherein the nucleic acid is in a vector.

20 39. The method according to claim 38, wherein the nucleic acid encodes an isoform of a human calcium sensing receptor, wherein the nucleic acid comprises about 2922 to about 3003 nucleotides and has a deletion of about 231 nucleotides when compared to the wild-type form of the receptor as depicted in SEQ ID NO:11.

40. The method according to claim 38, wherein said vector is selected from the group consisting of plasmids, retroviruses, herpes simplex viruses, adeno-associated viruses, adenoviruses, and vaccinia viruses.

25 41. The method according to claim 27, wherein the nucleic acid encodes an intracellular binding protein capable of binding a CaSR, or an isoform thereof.

42. The method according to claim 41, wherein the intracellular binding protein is an antibody or fragment thereof.

43. The method according to claim 42, wherein the antibody or fragment thereof binds the cytoplasmic domain of a CaSR.

30 44. The method according to claim 43, wherein the antibody or fragment thereof is a single chain antibody.

45. The method according to claim 41, wherein said nucleic acid further comprises a sequence encoding a localization signal for targeting the intracellular binding protein to the cellular location of a CaSR.

35 46. The method according to claim 45, wherein said localization signal is specific for the plasma

membrane.

47. The method according to claim 34, wherein said nucleic acid encodes an antisense molecule complementary to the sequence encoding a CaSR and capable of selectively inhibiting the expression of said sequence.
- 5 48. The method according to claim 47, wherein said antisense molecule is at least about 20 nucleotides in length.
49. An antigenic polypeptide comprising an an epitope and/or sequence not present in the wild-type CaSR, wherein said polypeptide elicits antibodies which bind to a CaSR isoform.
- 10 50. An antibody that specifically recognizes an isoform of CaSR, and does not bind the wild-type CaSR